

# PATENT ABSTRACTS OF JAPAN

(11)Publication number : 2003-065906

(43)Date of publication of application : 05.03.2003

---

(51)Int.Cl. G01N 1/00  
G01N 27/416  
G01N 27/447  
G01N 33/49  
// G01N 33/84

---

(21)Application number : 2001-304177 (71)Applicant : KIKUCHI JUN  
HORIIKE YASUHIRO  
(22)Date of filing : 23.08.2001 (72)Inventor : HORIIKE YASUHIRO  
OKI AKIO  
TAKAMURA ZEN  
OGAWA YOKI  
KIKUCHI JUN

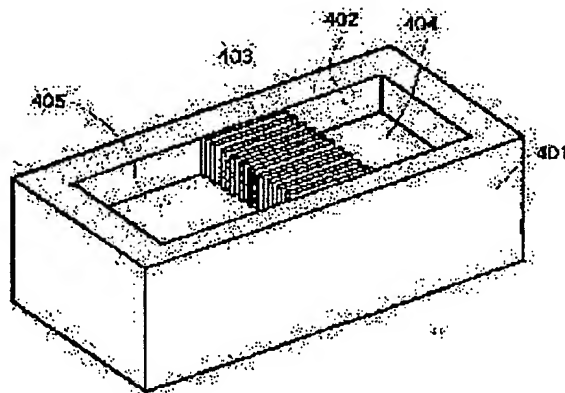
---

(54) LIQUID MOVING DEVICE, LIQUID COMPONENT ANALYZER AND METHOD FOR MANUFACTURING THEM

(57)Abstract:

PROBLEM TO BE SOLVED: To solve the problem that the capacity of an electroosmotic flow pump used for moving blood or the like is lowered because the zeta potential of the surface of a resin substrate is low in such a case that the resin substrate is used in order to inexpensively provide a liquid component analyzer including a blood analyzer and the high performance electroosmotic flow pump driven by low voltage inflicting no injury on a person is desired earnestly.

SOLUTION: A plurality of substrates comprising different materials are combined and integrated to constitute the liquid component analyzer.



Further, surface treatment is applied even to the substrates same in kind. Furthermore, a fine groove group is formed to an insulator or a substrate coated with an insulating material to realize a pump driven by low voltage.



---

## LEGAL STATUS

[Date of request for examination]

[Date of sending the examiner's decision of rejection]

[Kind of final disposal of application other than the examiner's decision of rejection or application converted registration]

[Date of final disposal for application]

[Patent number]

[Date of registration]

[Number of appeal against examiner's decision of rejection]

[Date of requesting appeal against examiner's decision of rejection]

[Date of extinction of right]

**\* NOTICES \***

JPO and NCIP are not responsible for any damages caused by the use of this translation.

1. This document has been translated by computer. So the translation may not reflect the original precisely.
2. \*\*\*\* shows the word which can not be translated.
3. In the drawings, any words are not translated.

---

**CLAIMS**

---

[Claim(s)]

[Claim 1] Slot passage is formed in an insulating material substrate. All over the slot passage concerned to the slot passage concerned and parallel And the grooves which consist of two or more [ have fixed die length in the same depth as the slot passage concerned ] are formed. By covering with the insulating material substrate which prepared the hole of a pair in the location corresponding to the both sides of the grooves concerned for the front face of the slot passage containing the grooves concerned, pouring in an electrolytic solution from the hole concerned, preparing an electrode in the hole of the pair concerned, and impressing an electrical potential difference to inter-electrode [ concerned ] Migration equipment of the electrolytic solution in the slot passage characterized by moving an electrolytic solution to another side from one side of two electrodes.

[Claim 2] Use a silicon substrate instead of the insulating material substrate concerned according to claim 1, and slot passage is formed in the silicon substrate concerned. The grooves which consist of two or more [ have fixed die length in the same depth as the slot passage concerned in parallel with the slot passage concerned ] are formed all over the slot passage concerned. By oxidizing all the front faces of the slot passage containing the grooves concerned, covering with the insulating material substrate which prepared the hole of a pair in the location corresponding to the both sides of the grooves concerned, pouring in an electrolytic solution from the hole concerned, preparing an electrode in the hole of the pair concerned, and impressing an electrical potential difference to inter-electrode / concerned Migration equipment of the electrolytic solution in the slot passage characterized by moving an electrolytic solution to another side from one side of two electrodes.

[Claim 3] Migration equipment of the electrolytic solution in the slot passage characterized by connecting to claims 1 and 2 the slot passage which makes the slot passage concerned move electric-field liquid to the upstream of the slot passage of a publication.

[Claim 4] The electrode which prepared the electrical potential difference impressed to the electrode of a pair given in claims 1 and 2 in the electrode ring of the upstream which an electrolytic solution moves is migration equipment of the electrolytic solution in the slot passage characterized by impressing an electrical potential difference to the electrode prepared in touch-down potential at the electrode ring of the downstream.

[Claim 5] The electrical potential difference impressed to the electrode of the downstream according to claim 4 is migration equipment of the electrolytic solution in the slot passage characterized by being - electrical potential difference.

[Claim 6] Migration equipment of the electrolytic solution in the slot passage characterized by processing a silicon substrate according to claim 2, changing the thickness of an oxide film after forming the slot passage concerned and two or more grooves, and changing the width of face between the slots of the two or more grooves concerned.

[Claim 7] Migration equipment of the electrolytic solution in the slot passage characterized by using silver/silver silver chloride electrode, and closing at the electrode of the upstream with which an electrolytic solution flows among the electrodes of the pair of a publication to claims 1 and 2.

[Claim 8] Migration equipment of the electrolytic solution in the slot passage characterized by for the two or more grooves concerned of a publication keeping spacing in claims 1 and 2, and being arranged at a serial.

[Claim 9] The two or more grooves concerned given in claims 1 and 2 are migration equipment of the electrolytic solution in the slot passage characterized by being arranged more widely than the width of face of the slot passage concerned, and connecting with the slot passage concerned.

[Claim 10] It is migration equipment of the electrolytic solution in the passage concerned according to claim 2 and the slot passage characterized by forming two or more grooves in the silicon layer on a SOI (Silicon Insulator) substrate.

[Claim 11] A silicon substrate and a silicon layer given in claims 2 and 10 are faced at formation of the slot passage concerned and two or more grooves. \*\*\*\* reactive ion etching for gas containing a fluorine atom, and fluorocarbon gas and the mixed gas of hydrogen are used. With floating potential Uniform deposition of Mizouchi of the fluorocarbon film, Removal of the pars-basilaris-ossis-occipitalis deposition film by \*\*\*\* reactive ion etching for gas containing a fluorine atom, The slot passage characterized by forming the structure concerned by repeating 1 cycle which consists of etching of silicon, and removal of the Mizouchi deposition film by the oxygen plasma many times, and the approach of two or more grooves formation.

[Claim 12] A silicon substrate and a silicon layer given in claims 2 and 10 are faced at formation of the slot passage concerned and two or more grooves. On the non-dense front face of the shape of a wave produced on the side attachment wall of all slots after the slot passage of claim 11, and etching formation of two or more grooves The gas which mixed the oxygen of 2.5 times or more of the gas concentration concerned in the gas containing a fluorine atom is made to discharge with 2.45GHz microwave. The silicon slot passage characterized by conveying the produced activity type of gas to the down-stream region where the plasma does not exist, and exposing it, and the approach of smoothing of the side attachment wall of two or more silicon grooves.

[Claim 13] The slot passage characterized by performing wet oxidation in case all the silicon front faces that include a silicon slot after smoothing of silicon slot passage according to claim 12 are oxidized, and the approach of two or more grooves formation.

[Claim 14] Component analysis equipment of the liquid constituted combining the components using two or more substrate ingredients with which the electrokinetic potentials in an interface with the solution concerned differ mutually when immersed in

the same electrolytic solution.

[Claim 15] Component analysis equipment of the liquid characterized by the electrokinetic potential in an interface with the solution concerned when being component analysis equipment of the liquid constituted combining two or more substrate components, surface treatment being performed to a part of front face [ at least ] of some substrates in two or more substrates concerned, and the front face after this surface treatment being especially immersed in the same electrolytic solution differing from it of the substrate ingredient before surface treatment.

[Claim 16] Component analysis equipment of the liquid characterized by using what contains especially a silicon oxide as a principal component as one of the substrate ingredients according to claim 14.

[Claim 17] the component analysis equipment of the liquid characterized by the silicon substrate front face concerned having oxidized by using especially silicon as a principal component as one of the substrate ingredients according to claim 14, using WA \*\*.

[Claim 18] Component analysis equipment of the liquid characterized by surface treatment according to claim 15 being covering of a silicon oxide film.

[Claim 19] The manufacture approach of the component analysis equipment of the liquid characterized by forming a silicon oxide film according to claim 18 using the plasma treatment of the gas of the molecule which contains silicon as a configuration element at least, and the gas of the molecule which contains oxygen as a configuration element, and the component analysis equipment of a liquid.

[Claim 20] The manufacture approach of the component analysis equipment of the liquid characterized by being reforming accompanying oxidation treatment of the molecule with which surface treatment according to claim 15 constitutes a front face, and the component analysis equipment of a liquid.

[Claim 21] Component analysis equipment of the liquid characterized by the substrate ingredient which performs surface preparation according to claim 15 being plastics.

[Claim 22] Component analysis equipment of the liquid characterized by using at least the plastics other than the substrate ingredient which contains silicon oxide according to claim 16 as a principal component as a substrate ingredient.

[Claim 23] Component analysis equipment of the liquid characterized by using the plastics other than the substrate ingredient which uses as a principal component the silicon with which the oxidizing zone is formed in the front face according to claim 17 as a substrate ingredient.

[Claim 24] Component analysis equipment of the liquid with which plastics according to claim 21 to 23 is characterized by being especially polyethylene terephthalate (PET).

[Claim 25] Component analysis equipment of the liquid with which plastics according to claim 21 to 23 is characterized by being especially a polycarbonate (PC).

[Claim 26] Especially a liquid given in claims 14 and 15 is component analysis equipment of the liquid characterized by hydrogen ion concentration being neutrality (pH being about seven).

[Claim 27] Especially a liquid given in claims 14 and 15 is component analysis equipment of the liquid characterized by being blood.

[Claim 28] An extraction means by which the component analysis equipment of a liquid according to claim 27 extracts blood from in the living body, Among separation means to separate a blood serum from a filtration means to filter the blood concerned extracted at

least and to obtain plasma, or the blood concerned, one of means, An analysis means to analyze the matter in the blood concerned, and the extraction means concerned, the filtration means concerned, the separation means concerned and a passage means to connect the analysis means concerned, The extraction means concerned, the filtration means concerned, the separation means concerned, the analysis means concerned, and the migration means to which the component of the blood concerned which exists in the passage means concerned is moved, Component analysis equipment of the liquid characterized by having a control means for controlling actuation of at least one means of the output means for taking out the information from the analysis means concerned outside, the extraction means concerned and the filtration means concerned, the separation means concerned, the analysis means concerned, the migration means concerned, and the output means concerned.

[Claim 29] Some means which include a migration means at least among various means according to claim 28, and other means are the manufacture approach of the component analysis equipment of the liquid which sticks them after being formed on a once different substrate, respectively, and is characterized by being unified, and the component analysis equipment of a liquid.

[Claim 30] Component analysis equipment of the liquid with which the substrate ingredient which forms the means of some which include a migration means at least according to claim 29 is characterized by using what contains especially a silicon oxide as a principal component.

[Claim 31] Component analysis equipment of the liquid characterized by the silicon substrate front face concerned having oxidized, using that in which the substrate ingredient which forms the means of some which include a migration means at least according to claim 29 contains especially silicon as a principal component.

[Claim 32] The substrate ingredient which forms the means of some which include a migration means at least according to claim 29 is especially plastics, and a migration means part is [ a front face ] component analysis equipment of the liquid characterized by mainly being covered with the silicon oxide film a part at least.

[Claim 33] The substrate ingredient which forms the means of some which include a migration means at least according to claim 29 is especially plastics, and a migration means part is [ a front face ] component analysis equipment of the liquid characterized by mainly being covered with the silicon oxide film a part at least.

[Claim 34] Component analysis equipment of the liquid characterized by giving reforming accompanying oxidation treatment of the molecule which constitutes a front face to a part of front face [ at least ] of the means of some which include a migration means at least according to claim 29.

[Claim 35] Especially plastics given in claims 33 and 34 is component analysis equipment of the liquid characterized by being polyethylene terephthalate.

[Claim 36] Especially plastics given in claims 33 and 34 is component analysis equipment of the liquid characterized by being a polycarbonate.

[Claim 37] Some [ at least ] front faces of the various means in the substrate which forms means other than the means of some which include a migration means at least according to claim 29 are the manufacture approaches of the component analysis equipment of the liquid characterized by being covered with the organic molecule which has biocompatibility, and the component analysis equipment of a liquid.

[Claim 38] Component analysis equipment of the liquid with which the organic molecule which has biocompatibility according to claim 29 is characterized by being especially an MPC (2-methacryloyloxyethylphorylcholine) polymer.

[Claim 39] It is component analysis equipment of the description and \*\*\*\*\* about the organic molecule which has biocompatibility according to claim 29 being especially a polyethylene glucose.

[Claim 40] Attachment of the substrates in which various means according to claim 29 were formed, and connection of each means of the substrate boundary accompanying unification are the manufacture approach of the component analysis equipment of the liquid characterized by carrying out by forming passage in the direction of a right angle in the connection side between other means, and the component analysis equipment of a liquid.

---

[Translation done.]

\* NOTICES \*

JPO and NCIP are not responsible for any damages caused by the use of this translation.

1. This document has been translated by computer. So the translation may not reflect the original precisely.
2. \*\*\*\* shows the word which can not be translated.
3. In the drawings, any words are not translated.

---

DETAILED DESCRIPTION

---

[Detailed Description of the Invention]

[0001]

[Field of the Invention] This invention relates to the chip equipment currently called the micro capillary constituted by the micro slot passage produced to insulating material substrates, such as a quartz plate and a macromolecule plate, its manufacture approach, and the pumping plant made to drive on an electrical potential difference low in order to move an electrolytic solution into the capillary concerned and its manufacture approach. Especially, electrolytic solutions, such as blood of a minute amount (one or less microliter), are poured in into a capillary, this is moved on the biosensor in a capillary, that component analysis measurement is performed, and it is related with the inspection diagnostic device and equipment which diagnose human being's health condition from this measurement result in the case of blood, and the electroendosmose style pumping plant to which an electrolytic solution is moved.

[0002]

[Description of the Prior Art] Conventional health and a conventional illness condition extracted a lot of several cc blood, and have been diagnosed from the measured value obtained with large-scale automatic hemanalysis equipment to the analysis. However, the ultra-fine processing technology used for semiconductor device production which progressed to the degree of pole is applied, various analyzers and an analysis apparatus are arranged on the chip of several cm around at most from several mm, body fluid, such as a test subject's blood, is led there, and development of the new device which can grasp a test subject's health condition in an instant, and the tendency of the utilization have been increasing in recent years. the site of that compression of the health insurance benefits an increment of which is enhanced can be aimed at because this makes the health care of old every day possible at home in this \*\*\*\* aging society with such the cheap advent of a device, or emergency medical service -- setting -- a test subject -- an infectious disease (hepatitis --) acquired immunodeficiency etc. -- etc. -- if it can judge quickly whether it holds or not using this device, since various social effectiveness is expected, that suitable correspondence can be performed etc. will be the technical field which is attracting attention very much.

[0003] Usually, such an automatic analyzer was installed in medical institutions, such as a hospital, the scale was large and the actuation was also restricted to what has special rating. However, such an automatic analyzer is replaced in recent years, and the small



simple hemanalysis approach and hemanalysis equipment which aimed at carrying out the hemanalysis by one's hand at each home are developed (application for patent 2000-120189).

[0004] An example of such hemanalysis equipment is shown in drawing 1. 101 is a substrate and each means of this equipment shown below is constituted by the micro capillary. 102 is the extraction means of blood. 103 is a needle in the air and is attached to an extraction means. 104 which stabs the inside of the body with this needle, and is used as the intake of the blood into a substrate, and 105 are electrodes, and take in blood in a substrate from the inside of the body with the suction force by the electroendosmose style produced for the electrical potential difference impressed to inter-electrode [ this ]. 106 is the filtration means of blood and has two or more slits which become narrow [ spacing ] gradually toward a lower stream of a river from the upstream of the flow of blood. By this slit, the erythrocyte in blood, a leucocyte, a lymphocyte, and a platelet are filtered and removed, and plasma is obtained to the downstream of a filtration means. 107 is a separation means, for example, consists of a micro capillary of a U character mold. After leading the plasma which filters the extracted blood and is obtained to this U character type of micro capillary, the blood serum which carried out separation removal of the coagulation factor from plasma is obtained by the U character section by applying acceleration in the fixed direction for this substrate with a centrifugal separation vessel. 108 is an analysis means and has a sensor for measuring each concentration, such as the pH value in blood, oxygen, a carbon dioxide, sodium, a potassium, calcium, a glucose, and a lactic acid. 109 is a passage means to connect each of an extraction means, a filtration means, a separation means, and an analysis means, and consists of a micro capillary which etched and manufactured the substrate. 110 is a migration means for moving blood by the electroendosmose style in a micro capillary. 111 is an output means for taking out information from an analysis means, and consists of electrodes etc. 112 is a control means for controlling the above extraction means, a filtration means, a separation means, an analysis means, a migration means, and an output means if needed. Although not illustrated, it has a maintenance means for holding blood in the micro capillary on a substrate, and this plate is pasted up or stuck to the substrate 101 by pressure.

[0005] It is filtered with the filtration means 104 and becomes plasma, and separation removal of the coagulation factor is further carried out with the separation means 105, a blood serum is obtained, and the blood extracted by the extraction means 102 measures each concentration, such as a pH value, oxygen, a carbon dioxide, sodium, a potassium, calcium, a glucose, and a lactic acid, for this in an analysis means. The migration means 110 which used the electrophoresis method performs migration of the blood between each means.

[0006] Although glass ingredients, such as a quartz, were used for the substrate of such hemanalysis equipment in many cases, a resin material is increasingly used as what is suitable holding down costs and manufacturing equipment in large quantities again.

[0007] Moreover, the migration means 110 stated by drawing 1 is used in order to draw blood in a micro micro capillary chip or to introduce the solution for proofreading of a biosensor, is micro and consists of pumps of a low power drive. Although what drove diaphragm with the PIESO component with the micro machine technique is main as for the conventional micro pump In addition, an electrode array is inserted into that to which the

molecule which puts in a mesh electrode in a capillary, impresses a high DC electrical potential difference to this, and has a charge in an electrolytic solution is driven, and a solution is moved, and a capillary. The electrical potential difference of a square wave is impressed carrying out a phase shift to it, and there are some to which an electrolytic solution is moved.

[0008]

[Problem(s) to be Solved by the Invention] since the absolute value of the electrokinetic potential (  $F$ -potential ) of the front face when dip the almost neutral solution containing a blood blood serum component element be comparatively low when a resin material be use as a substrate , if the capacity of the pump action in a migration means 110 to use an electroendosmose style decline , the problem acquire and say have arise . On the other hand, in order to suppress adhesion of protein and a corpuscle, it is necessary to cover the macromolecule micell which has the straight chain of the organic material which has biocompatibility, for example, an MPC (2 methacryloyloxyethylphorylcholine) polymer, and a polyethylene glycol (PEG) on a front face with the part which the whole blood or the blood serum of the extraction means 102, the filtration means 106, the separation means 107, the analysis means 108, and the passage means 109 contacts on a front face. The effectiveness of these living body adaptation film is already described in the application for patent 2000-116091.

[0009] In order to solve these problems, the front face of the extraction means 102 in the means of the versatility on the same resin substrate as shown in drawing 1 in the application for patent 2000-116091, the filtration means 106, the separation means 107, the analysis means 108, and the passage means 109 is covered with the organic material which has biocompatibility. An ingredient with the large absolute value of the  $F$ -potential of a front face when the front face of the migration means 110 dips a neutral electrolytic solution on the other hand, For example, it covers with a silicon oxide partially, or the method of aiming at reforming of the resin which constitutes the migration means front face concerned, and raising the absolute value of  $F$ -potential by plasma treatment, is shown. However, in the case of these approaches, covering or surface treatment of a desired ingredient needed to be performed to the desired part, but since the magnitude of each means on a substrate was the order of the micrometer from the first, there was a problem that it was difficult to perform classification and surface treatment of covering of such a front face with a sufficient precision.

[0010] Moreover, the diaphragm drive of the micro pump used conventionally is complicated structure, a life is also in diaphragm, and we are anxious also about making blood and an electrolytic solution pollute depending on the quality of the material. Moreover, it is not so easy on manufacture to prepare an electrode in the part to which other solutions are moved, and it also has the problem of the same contamination. Although the chip which can diagnose health condition by being home which this invention aims at must be the cheap thing which can be thrown away, since it cannot say that the conventional approach is cheap but the high voltage and a RF are needed further, people cannot call it insurance for using it at home. The purpose of this invention has structure in offering the electroendosmose style pumping plant to which an electrolytic solution can be simply moved powerfully by low-battery drive, in order to pour minute amount blood into a micro capillary chip using a super-thin needle.

[0011]

[Means for Solving the Problem] The trouble at the time of performing covering or surface treatment of a desired ingredient to the part of a request of the conventional technique which was expressed in the top forms various means on the same substrate, and derives them from having performed surface treatment suitably required for a part of these front faces. The artificers of this invention changed many divisions of \*\*\*\*\* and substrates used for every them for every required surface treatment, formed these means, respectively, after they performed required surface treatment, stuck these substrates, unified, and they thought that what is necessary was just to constitute hemanalysis equipment. For example, in drawing 1, the means of the extraction means 102, the filtration means 106, the separation means 107, the analysis means 108, and passage means 109 grade and the migration means 110 are produced independently of on a respectively different substrate, and both are stuck and it unifies, after giving appropriate surface coating, surface treatment, etc. to each substrate. There is an advantage that covering or the reformer, and the approach that it becomes unnecessary to perform surface coating and surface treatment locally like before, and special time and effort is needed are not needed, by doing in this way.

[0012] The means of extraction means 102 other than migration means 110, the filtration means 106, the separation means 107, the analysis means 108, and passage means 109 grade is formed on the cheap substrate made of resin concrete first. A part of front face [ at least ] which constitutes these means at this time is covered with the ingredient which has biocompatibility, such as an MPC polymer. On the other hand, the migration means 110 is formed on a substrate with surface area smaller than the above-mentioned substrate made of resin. When a part of front face [ at least ] which constitutes the migration means 110 at least at this time dips the electrolytic solution of a neutral region, it consists of ingredients with the absolute value of F-potential higher than that of the front face of the various means formed on the above-mentioned substrate made of resin. And the substrate made of these resin and the substrate with which the migration means 110 is formed are stuck, and it unifies. At this time, passage is certainly connected between the analysis means 108 on a resin substrate, and the migration means 110 on a substrate with surface area smaller than the resin substrate concerned. Adhesion of protein, various corpuscles, etc. which are contained in a constituent of blood by making it above in the means of the extraction means 102, the filtration means 106, the separation means 107, the analysis means 108, and passage means 109 grade is controlled. A blood blood serum component can pass these means duly. Moreover, a part of front face [ at least ] of the migration means 110 From consisting of ingredients with the absolute value of F-potential higher than that of the front face of the various means formed on the above-mentioned substrate made of resin, when the electrolytic solution of a neutral region is dipped When using an electroendosmose style as a migration means, high drawing in or extrusion capacity can be acquired with low inter-electrode potential.

[0013] Moreover, the principle of an electroendosmose style used as some radicals of this invention is briefly explained using drawing 2. Although 201 is a quartz plate and the quartz front face 202 is usually covered with the hydroxyl group, if an electrolytic solution 203 is poured into the capillary 204 made from a quartz, a hydrogen ion moves into an electrolytic solution, consequently negative charge 205 arises on the surface of a quartz, and the cation 206 in an electrolytic solution (cation) will move to a front face, and will produce the electric double layer 207 of helmholtz. An electroendosmose style

has the large one where F-potential, and a call and its potential are larger in this potential, and that potential of especially a quartz is high. then, the both ends of a capillary -- forward -- 208 and negative -- when the high voltage of 209 is impressed, the phenomenon which the cation flows to a negative electrical-potential-difference side, and the electrolytic solution itself moves in the negative electrical-potential-difference direction by the viscous flow 210 is an electroendosmose style. Therefore, if such a capillary made from a quartz is connected to a part of passage, an electrical potential difference is impressed only to the both ends of a capillary and passage is filled with an electrolytic solution, an electrolytic solution can be moved to the whole passage by the electroendosmose style which flows to the capillary. The thing equivalent to this capillary made from a quartz is calling it the electroendosmose style pump. However, in order to move an electrolytic solution, hundreds to several kV was also required only by impressing an electrical potential difference to a part of passage like drawing 2 conventionally. Since the pressure to which the electrolytic solution equivalent to electroendosmose style pump capacity is moved on the other hand is mostly in inverse proportion to the cross section of a capillary, since adhesion of a cation is increased, width of face is wide, in order that a solution may make it easy to flow, die length is short, and in order for high electric field to make it impressed only by the pump part, the structure of a narrow gap is needed.

[0014]

[Embodiment of the Invention] The schematic diagram of the equipment based on this invention is shown in drawing 3. The same number as drawing 1 shows the thing same all over drawing as drawing 1. The means of the extraction means 102, the separation means 107, the analysis means 108, and passage means 109 grade is formed between the resin substrate A303 and the resin substrate B304, and these front faces are covered with the MPC polymer. On the other hand, the migration means 110 is formed between a substrate A306 and a substrate B307, and when a part of front face [ at least ] of the migration means concerned dips the electrolytic solution of a neutral region, it consists of ingredients with the absolute value of F-potential higher than that of the front face of the various means formed on the above-mentioned substrate made of resin. [ at least ] This may use an ingredient with F-potential high in this way for the substrate itself, may cover the front face with an ingredient with high F-potential using cheap resin to a substrate, and may raise F-potential by surface treatment processing. After performing such processing, the resin substrate A303, the resin substrate B304, and a substrate A306 and a substrate B307 are stuck, and it unifies. The passage between the analysis means 108 and the migration means 110 is connectable by sticking making the hole which the resin substrate A303 and the substrate B307 were made to penetrate in the passage connection 302 at this time agree.

[0015] The schematic diagram of the structure of the electroendosmose style pump of this invention is shown in drawing 4. 401 is an insulating material plate or silicon substrates, such as a quartz plate, 402 is the slot passage used as a micro capillary, the trench group which becomes the part from the a large number book of 403 is formed, and 404 and 405 are an inlet and emission opening, respectively. In the case of a silicon substrate, 402 and 403 are first oxidized after processing formation. Drawing 5 is the lid 501 of the substrate with which the slot shown by drawing 4 was formed, and oxidizes a quartz substrate or a silicon substrate. 401 and 501 are pasted up. 502 and 503 are the

holes the inlet of an electrolytic solution, and for emission openings corresponding to 404 and 405, respectively, and 504 and 505 are electrodes, respectively and are a metal, a linear Ag/AgCl electrode, or linear metal thin films, such as platinum.

[0016] Next, signs that the pump action of this invention is caused in structure are explained to drawing 4 using drawing 6. First, a flute width is narrow, and the depth is the same depth as slot passage, and forms the grooves 602 which prepared the several many slots in a part of slot passage whole [ 601 ] where an electrolytic solution flows. And if an electrolytic solution is filled to the whole slot passage and an electrical potential difference is impressed to the both sides of these two or more grooves from the electrode of 603 and 604, ion tends to flow, in the part 602 of grooves, it will be hard to flow and resistance will become very high 605 and 606 other than these grooves. Therefore, as the great portion of applied voltage concentrates on the both ends of grooves, consequently it is shown in drawing 6, since high electric field will be impressed to the narrow slot gap in grooves, even if the electrical potential difference which the cation adhering to a slot impressed is low, it becomes easy to move electric field 607.

[0017]

[Example] The [first example] In drawing 2, polyethylene terephthalate (PET) is used as an ingredient of the resin substrates A, B, and C. Moreover, the extraction means 102, the separation means 107, the analysis means 108, and the means of passage means 109 grade and the migration means 110 which used the electroendosmose style are formed on each substrate, using a quartz as an ingredient of the substrate ingredients A and B. After covering an MPC polymer in the front face of each means on a PET substrate, the lamination unification of a PET substrate and the quartz substrate is carried out, and hemanalysis equipment is constituted. It checked that a phosphate buffer solution is filled only in a migration means, blood was actually drawn from the extraction means 102 using an electroendosmose style, the separation means 107 performed blood serum corpuscle separation, and it could perform leading a blood serum component to an analysis means in a short time rather than the case where migration of blood and a constituent of blood produces satisfactory only using a quartz substrate when tried. It is thought that it is because are the process which covers an MPC polymer only for the extraction means 102 of drawing 1, the separation means 107, the analysis means 108, and the passage means 109, the solvent which contains an MPC polymer slightly permeated to the migration means 110, a part of here will be covered with an MPC polymer and F-potential fell that it can be made to move for a short time rather than the case of only a quartz substrate. Thus, an analysis apparatus including the migration means of a liquid is cheaply producible, controlling the problem accompanying such surface treatment by making into plurality the substrate used according to a required surface state by this invention. Moreover, the migration means 110 was formed in the front face in which a silicon substrate is oxidized thermally and the total dinner lower layer is formed, and when it stuck with this and the PET substrate in which the means of the extraction means 102, the separation means 107, the analysis means 108, and passage means 109 grade was formed and unified, the almost same good result was obtained.

[0018] The [second example] PET which is cheap plastics is used as a substrate instead of the quartz substrate used in the first example. After forming a migration means in this, for the purpose of silicon oxide-film covering to this wall front face as the molecule which contains silicon as a configuration element in a migration means -- TEOS (a

tetra-ethoxy silane --) Introduce oxygen with the helium (helium) as a diluent as a molecule which contains Si (OC<sub>2</sub>H<sub>5</sub>)<sub>4</sub> and oxygen as a configuration element, and an electrode is installed in the substrate outside of a migration means. The RF (frequency: 13.56MHz) was impressed to this 5W, and the microplasma was generated under the atmospheric pressure within a migration means. After performing this processing for 1 minute, it sticks with the PET substrate in which the extraction means 102, the separation means 107, the analysis means 108, and the passage means 109 were formed, and unifies, and hemanalysis equipment is formed. It checked that blood was actually drawn from the extraction means 102, the separation means 107 performed blood serum corpuscle separation, and migration of the blood and the constituent of blood of leading a blood serum component to an analysis means could be performed satisfactory. Moreover, after introducing the oxygen gas diluted with helium and performing microplasma processing in a migration means similarly, blood almost equivalent to the case where introduced TEOS and a silicon oxide film is covered to a wall, and the migration property of a constituent of blood were acquired. This is considered to be because for high F-potential to have been obtained as a result of the polarization of the molecule which constitutes a front face by surface treatment processing to which a wall front face oxidizes by the oxygen plasma. The good result was obtained as well as the time of PET when the polycarbonate (PC) which is too still cheaper plastic material instead of PET was used.

[0019] The [third example] The electroendosome style pump as shown in drawing 4 was produced, and the engine performance was investigated. In the case of the quartz plate, the producing method carried out sputter deposition of the chromium (Cr) film to the quartz plate front face by the thickness of 1.5 micrometers using the quartz plate and the silicon substrate. In the case of silicon, wet oxidation of the silicon substrate was carried out at 1000 degrees C, and it formed the 800nm thermal oxidation film. On Cr film, in the case of silicon, in the case of the quartz plate, about 700nm spin spreading of the electron beam resist (ZEP7000) was carried out, and it formed the pattern with the electron-beam-lithography machine on the oxide film. It was laid in the mask, in the case of Cr film, the wafer was laid in the water-cooled base which switched on 13.56MHz high-frequency power for ICP (inductively coupled plasma) by 500kW at the one-roll antenna mold, and combined the mixed gas of +30% oxygen of chlorine with the 13.56MHz RF for DC-bias impression from the antenna in the location of a 19cm lower stream of a river, and Cr film was etched by 120eV ion energy. ICP of SF<sub>6</sub> was used for the mask for this Cr film C3F<sub>8</sub>+70%, and the quartz substrate of a substrate was etched.

[0020] Using C<sub>4</sub>F<sub>8</sub>+40%H<sub>2</sub>, in the case of the thermal oxidation film, 13.56MHz high-frequency power was supplied to the one-roll antenna of ICP by 600kW, it laid the wafer in the water-cooled base combined with 13.56MHz high frequency for DC-bias impression, and etched it with this resist mask by 300eV ion energy. After removing a resist, the oxide film was used as the mask and Si substrate of a substrate was etched with the amelioration Bosch process. The usual Bosch process etches Si into an isotropic configuration with plasma, such as (1) SF<sub>6</sub>. (2) By plasma, such as CHF<sub>3</sub>, impress the fluorocarbon film to the wall of an isotropic configuration, and high frequency bias is impressed to a base in deposition and (3) argon plasma. Although the impact of the Ar<sup>+</sup> ion is carried out, 1 cycle of removal of only the deposition film at the bottom is repeated many times and Fukahori (deep) etching of Si substrate is performed, sputter



etching of the thermal oxidation film is carried out with Ar<sup>+</sup> ion and mask-proof nature is \*\*\*\*\*. Then, although an undercut 702 will arise as this amelioration if (1) silicon oxide film 701 is first used as a mask and RIE (reactive ion etching) using SF<sub>6</sub> is performed as that process is shown in drawing 7, more partes basilaris ossis occipitalis 703 than the amount of undercuts are etched. Here, 704 is a silicon substrate. (2) Make Mizouchi deposit the fluorocarbon film 705 on homogeneity in floating potential using C<sub>4</sub>F<sub>8</sub>+20%H<sub>2</sub>. (3) Etch the silicon substrate 704 of a substrate into the coincidence which removes the pars-basilaris-ossis-occipitalis deposition film according to the process of (1) again. (4) O<sub>2</sub> plasma removes the Mizouchi deposition film. 1 cycle which consists of this process is repeated many times, and a silicon substrate is etched deeply. However, it originates in the undercut of 703 and a wavelike configuration essentially occurs on a slot side attachment wall. Then, with the fluorine atom produced in the 2.45GHz microwave discharge using O<sub>2</sub> 4+300% of CF<sub>4</sub>, and a superfluous oxygen atom, this slot is processed by the downflow and a wavelike configuration is graduated. All front faces including the slot on the silicon are oxidized after the process concerned. although an oxide film is risen and formed in opening of a slot by the dry oxidation using O<sub>2</sub> in that case as shown in drawing 8 (b) -- the pie ROJIE nick reaction of the steam of distilled water, the mixed gas of oxygen, and the mixed gas of oxygen and hydrogen -- \*\*\*\* -- when the wet oxidation style which introduces the produced water into a hot electric furnace, and oxidizes silicon was used, it became clear that Mizouchi oxidized to homogeneity as shown in drawing 8 (b).

[0021] In this way, 2/13 kind of wet oxidation was considered for the formed silicon slot as 10 minutes at 1000 degrees C. This slot passage, the chip which consists of grooves, and the quartz plate which opened the electrode ring with the ultrasonic drill were immersed into 1% fluoric acid solution, and the pressure of 1.3Mpa was impressed for 24 hours, and it pasted up. This is calling it fluoric acid bonding. Since manufacture of a deep groove with a width of face of 1 micrometer or less was difficult in the case of the quartz substrate, drawing 9 shows the block diagram when investigating the engine performance using the electroendosome style pump manufactured to the silicon substrate. The grooves pump section 904 which formed the Ag/AgCl electrode 902 and the platinum electrode 903 in the electrode ring with a diameter [ of the both sides of the slot passage 901 with a width of face / of 0.5mm / and a depth of 10 micrometers ] of 1.5mm, and established the SiO<sub>2</sub>/Si slot with a gaps [ two kinds of ], 0.85 micrometers (a) and 0.6 micrometers (b), and a depth of 10 micrometers in the 0.5mmx0.5mm field in the meantime at 316 trains was produced. + electrical potential difference was impressed to the Ag/AgCl electrode of 902, and - electrical potential difference was impressed to the platinum electrode of 903. The reason using an Ag/AgCl electrode is that there is no phenomenon of electrolyzing an electrolytic solution in impression of a low battery, and generating hydrogen. Therefore, it stopped the hole with adhesives after inserting an Ag/AgCl electrode in order to prevent the inflow of the air from the hole of 902, since the flow of an electrolytic solution flows toward 902 to 903. Spacing of the hole of 902 and 903 is 3mm, and moved the electrolytic solution of the 3mmx10micrometerx0.5mm volume as a load after all. As an electrolytic solution, ionic strength used 1/10 and pH used PBS (phosphate buffer solution) of 7.4. In case blood is drawn in a capillary 906 from the inlet of 905 and a health marker is measured using the pump concerned with a reference electrode 907 and a biosensor (ion sensitive electric-field mold transistor) 908,

for example, ISFET, in order to prevent the effect of the potential impressed to the electrostatic discharge and the pump concerned of gate dielectric film of ISFET, the Ag/AgCl electrode of 902 is made into touch-down potential.

[0022] Drawing 10 shows the relation between a flow rate (a nano liter / second) and applied voltage using the pump made from this silicon substrate. (a) was the case where the gap between slots was 0.85 micrometers, and the flow rate increased almost in [ 10V ] linearity, and it showed the inclination of saturation after that. Since the thickness of the film which oxidized Si was 200nm and the electric field of  $5 \times 10^4$  V/cm were impressed to the oxide film by impression of 10V, current leak of an oxide film or a part of dielectric breakdown arise, and since applied voltage fell, this is considered. However, the 0.5 nano l. [ /second ] rate of flow is acquired for PBS of said volume on the electrical potential difference of 10V, and this has the force which makes water height of 25mm. Proof-pressure degradation can improve by thickening oxide-film thickness, (b) is the case where the gap between slots is 0.6 micrometers, and both pressure-proofing and its flow rate are improving. if this grooves mold is called a vertical mold — as a comparison — the inside of drawing 10 — width-of-face [ of 1mm ], die-length [ of 100 micrometers ], and gap 0.85micrometer — the result of having carried out dry etching processing and having produced the electroendosome style pump of the structure called a monotonous mold to the quartz plate was shown as (c). Consequently, if the pump force in 0.85 micrometers of the same gap is measured, it will be thought that the vertical mold is excellent in the applied voltage of 10V about 10 times compared with a flat-surface mold.

[0023] The [fourth example] In order to also use the flat-surface section of the vertical mold of drawing 4 , the thing of the structure which combined the monotonous mold shown in a vertical mold and drawing 10 is shown in drawing 11 . In this case, an electrolytic solution flows to space and a perpendicular direction. As for electric insulating plates, such as a quartz with which 1101 forms slot passage and grooves, a silicon substrate, and 1102, grooves and 1103 are electric insulating plates and silicon substrates, such as a quartz, and the monotonous slot 1104 is processed into the part. In the case of a silicon substrate, it oxidizes like the above-mentioned. The above-mentioned fluoric acid bonding is carried out to adhesion of the substrate of 1101 and 1103. About 10% of pump force was able to be made to increase according to the structure concerned compared with the mere ditch type of drawing 2 .

[0024] Drawing 12 is deformation of this example, first, forms the slot 1201 of a monotonous mold in the insulating material substrate and silicon substrate like a quartz plate, and covers them with many lids for these grooves 1202 with \*\*\*\*\* and the insulating material substrate 1203 into it. Effectiveness was the same as the structure of drawing 9 .

[0025] The [fifth example] Since drawing 13 increases the pump force further, the structure which made plurality the a large number book grooves shown in drawing 4 , opened spacing, and was connected to the serial is shown. 1301 is slot passage and the capillary passage as a load with which an electrode ring and 1304 draw grooves and, as for 1302 and 1303, 1305 draws blood etc. Even if it uses two or more slots concerned and the slot of the same die length, naturally the pump force improves, but when the ion current flows such a long slot, Joule heating happens, a pump may be damaged or a foreign matter may be got blocked in a thin slot. Therefore, these problems divided slot



structure and have solved it by making it a serial.

[0026] The [sixth example] Drawing 14 shows the increase of the number of the slots on the grooves, and the pump structure which opened spacing in the serial and was connected still like drawing 10 in the slot structure of drawing 4 aiming at improvement in the pump force. Taper structure for an electrolytic solution to impress a sink and electric field gently smoothly to the a large number book grooves of the slot passage of 1401 to 1404, as for the grooves to which slot passage, and 1402 and 1403 increased the electrode ring, and 1401 1404 increased the number of slots, and 1405, and 1406 are the capillary passage as a load which draws blood etc. In this example, the still bigger pump force was able to be acquired by connecting plurality to a serial for single a large number book grooves like drawing 13 .

[0027] The [seventh example] By the result of the structure which oxidized the silicon slot shown in drawing 10 , if pressure-proofing of an oxide film is bad, the pump force will be saturated with current leak etc. to electrical-potential-difference impression. As for saying [ that leak produces this cause in an oxide film ], the potential of an electrolytic solution and the silicon substrate of a substrate means approach or becoming the same. In order to prevent this, the slot structure using a SOI (Silicon on Insulator) substrate is shown in drawing 15 that the silicon substrate should just be floating [ therefore ] electrically. For a silicon oxide film and 1503, as for a silicon oxide film and 1505, in drawing 15 , a silicon layer and 1504 are [ 1501 / a silicon substrate and 1502 / grooves and 1506 ] the lids of a silicon oxide film. The flow rate increased in linearity, without being saturated with using the SOI substrate concerned, as shown in drawing 16 even if it could enlarge pressure-proofing further and impressed 20V.

[0028]

[Effect of the Invention] The component analysis equipment of the electrolytic solution containing cheaply highly efficient blood was realizable by combining two or more substrates by this invention as explained above. Moreover, high performance-ization of the electroendosmose style pump which is the important component of the equipment concerned was able to be attained. It became possible to use for cheapness and the body at insurance the device which diagnoses health condition etc. from minute amount blood at home by this. Furthermore, this invention did not stop only at blood but has contributed also to the component analysis equipment of a minute amount liquid.

---

[Translation done.]

\* NOTICES \*

JPO and NCIP are not responsible for any damages caused by the use of this translation.

1. This document has been translated by computer. So the translation may not reflect the original precisely.
2. \*\*\*\* shows the word which can not be translated.
3. In the drawings, any words are not translated.

---

## DESCRIPTION OF DRAWINGS

---

### [Brief Description of the Drawings]

[Drawing 1] It is drawing which explains equipment conventionally.

[Drawing 2] It is drawing which the principle of an electroendosmose style used as some radicals of this invention explains.

[Drawing 3] It is the schematic diagram of the equipment by this invention.

[Drawing 4] It is the schematic diagram of the structure of the electroendosmose style pump which consists of the slot passage and two or more grooves of this invention.

[Drawing 5] It is the lid of the insulating material of the substrate with which the slot passage shown by drawing 4 and two or more grooves were formed, and the structure which inserted the electrode in the inlet and the object for emission openings of an electrolytic solution, respectively is shown.

[Drawing 6] It is drawing explaining electric field strong against the gap of the two or more slot used as the radical which produces a powerful electroendosmose style operation in the two or more grooves of this invention in structure at drawing 2 arising.

[Drawing 7] It is drawing explaining the etching process which makes the four processes concerned 1 cycle and repeats them many times as an etching method which improved the Bosch process which forms a trench in a silicon substrate.

[Drawing 8] In case a silicon slot is oxidized, it is drawing having shown the difference in signs that O<sub>2</sub> dry oxidation is formed of wet oxidation, as for (b), and an oxide film is formed, as for (b).

[Drawing 9] The block diagram for investigating the engine performance of the electroendosmose style pump by the a large number book grooves manufactured to the silicon substrate is shown.

[Drawing 10] The relation between a flow rate and applied voltage is shown using the electroendosmose style pump (here, it is called the vertical mold) by the a large number book grooves manufactured to the silicon substrate. (a) is the case where the gaps between slots are 0.85 micrometers and 0.6 micrometers, and (c) shows the property of the structure of the flat-surface mold shown all over drawing.

[Drawing 11] The pump of the structure which combined the vertical mold and the monotonous mold is shown.

[Drawing 12] It is drawing showing the example of transformation of drawing 11.

[Drawing 13] The structure which made a large number book grooves plurality, opened spacing, connected with the serial, and aimed at pump force enhancement is shown.

[Drawing 14] In the slot structure of drawing 4 , the increase of the number of the slots on the grooves and the structure which opened spacing in the serial still like drawing 10 , and aimed at connection pump force enhancement are shown.

[Drawing 15] When a majority of these grooves are formed in the silicon layer using a SOI (Silicon on Insulator) substrate, even if leak exists in a silicon oxide film, the pump structure where the high voltage can be impressed is shown.

[Drawing 16] It is drawing showing the electroendosmose style property using the a large number book grooves shown in drawing 15 .

[Description of Notations]

- 101 Substrate
- 102 Extraction Means
- 103 Needle
- 104 Electrode
- 105 Electrode
- 106 Filtration Means
- 107 Separation Mechanism
- 108 Analysis Means
- 109 Passage Means
- 110 Migration Means
- 111 Output Means
- 112 Control Means
- 201 Quartz Plate
- 202 Quartz Front Face
- 203 Electrolytic Solution
- 204 Capillary made from Quartz
- 205 Negative Charge
- 206 Cation
- 207 Electric Double Layer of Helmholtz
- 208 Forward Electrode
- 209 Negative Electrode
- 210 Viscous Flow
- 301 Liquid Reservoir
- 302 Passage Connection
- 303 Resin Substrate A
- 304 Resin Substrate B
- 305 Resin Substrate C
- 306 Substrate A
- 307 Substrate B
- 401 Quartz Plate
- 402 Slot Passage
- 403 Grooves
- 404 Inlet
- 405 Emission Opening
- 501 Lid
- 502 Hole for Inlets
- 503 Hole for Emission Openings

504 Electrode  
505 Electrode  
601 Slot Passage Whole  
602 Grooves  
603 Electrode  
604 Electrode  
605 Slot Passage other than Grooves  
606 Slot Passage other than Grooves  
607 Electric Field  
701 Silicon Oxide Film  
702 Undercut  
703 Pars Basilaris Osis Occipitalis  
704 Silicon Substrate  
705 Fluorocarbon Film  
801 Silicon Oxide Film  
802 Silicon Substrate  
901 Slot Passage  
902 Ag/AgCl Electrode  
903 Platinum Electrode  
904 Grooves Pump Section  
905 Inlet  
906 Capillary  
907 Reference Electrode  
908 ISFET  
1101 Substrate  
1102 Grooves  
1103 Substrate  
1104 Slot  
1201 Slot  
1202 Large Number Book Grooves  
1203 Substrate  
1204 Substrate  
1301 Slot Passage  
1302 Electrode  
1303 Electrode  
1304 Grooves  
1305 Capillary Passage  
1401 Slot Passage  
1402 Electrode  
1403 Electrode  
1404 Grooves  
1405 Taper Structure  
1406 Capillary Passage  
1501 Silicon Substrate  
1502 Silicon Oxide Film  
1503 Silicon Layer

1504 Silicon Oxide Film ●  
1505 Grooves  
1506 Lid of Silicon Oxide Film ●

---

[Translation done.]

(19)日本国特許庁 (J P)

(12) 公 開 特 許 公 報 (A)

(11)特許出願公開番号

特開2003-65906

(P2003-65906A)

(43)公開日 平成15年3月5日(2003.3.5)

(51)Int.Cl. <sup>7</sup>	識別記号	F I	テ-マ-ト*(参考)
G 0 1 N 1/00	1 0 1	G 0 1 N 1/00	1 0 1 F 2 G 0 4 5
27/416		33/49	Z 2 G 0 5 2
27/447		33/84	A
33/49			Z
// G 0 1 N 33/84		27/26	3 3 1 G

審査請求 未請求 請求項の数40 巻面 (全 12 頁) 最終頁に続く

(21)出願番号 特願2001-304177(P2001-304177)

(22)出願日 平成13年8月23日(2001.8.23)

(71)出願人 599153220

菊地 純

東京都港区白金台2丁目14番地6号

(71)出願人 594169385

堀池 靖浩

東京都西東京市東伏見3丁目2番地12号

(72)発明者 堀池 靖浩

東京都西東京市東伏見3丁目2番地12号

(72)発明者 沖 明男

東京都三鷹市大沢二丁目20番地33 第二武蔵野寮418号

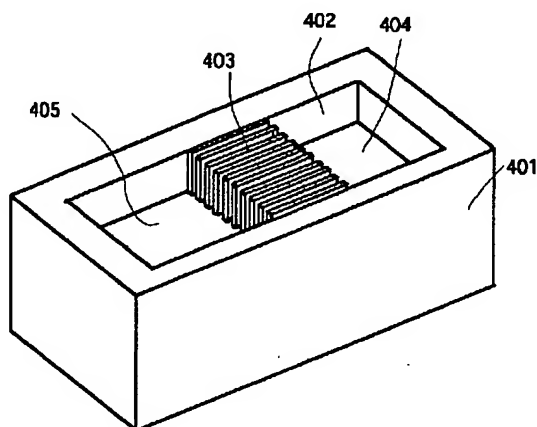
最終頁に続く

(54)【発明の名称】 液体の移動装置と液体の成分分析装置ならびにそれらの製造方法

(57)【要約】

【課題】安価に血液分析装置を含む液体の成分分析装置を提供するために樹脂基板を用いた場合、その表面のゼータ電位が低いために血液等を移動させるために用いる電気浸透流ポンプの能力が低下してしまう。また人に危害のないような低電圧駆動の高性能な当該ポンプが切望されていた。

【解決手段】材質の異なる複数の基板を組み合わせてこれらを一体化し、液体の成分分析装置を構成する。また同一種類の基板でも表面処理を施す。また微細な溝群を絶縁体あるいは絶縁体被覆を施した基板上に構成し、低電圧駆動のポンプを実現する。



## 【特許請求の範囲】

【請求項1】絶縁材基板に溝流路を形成し、当該溝流路中に当該溝流路と平行に、且つ当該溝流路と同じ深さで一定の長さを有する複数本からなる溝群を形成し、当該溝群を含む溝流路の表面を、当該溝群の両側に対応する位置に一对の孔を設けた絶縁材基板で蓋をし、当該孔から電解質溶液を注入し、当該一对の孔に電極を設け、当該電極間に電圧を印加することにより、両電極の一方から他方に電解質溶液を移動させることを特徴とした溝流路内での電解質溶液の移動装置。

【請求項2】請求項1に記載の当該絶縁材基板の代わりに珪素基板を用い、当該珪素基板に溝流路を形成し、当該溝流路中に当該溝流路と平行に、且つ当該溝流路と同じ深さで一定の長さを有する複数本からなる溝群を形成し、当該溝群を含む溝流路の全表面を酸化し、当該溝群の両側に対応する位置に一对の孔を設けた絶縁材基板で蓋をし、当該孔から電解質溶液を注入し、当該一对の孔に電極を設け、当該電極間に電圧を印加することにより、両電極の一方から他方に電解質溶液を移動させることを特徴とした溝流路内での電解質溶液の移動装置。

【請求項3】請求項1及び2に記載の溝流路の上流に、電界液を当該溝流路に移動させる溝流路が接続されていることを特徴とする溝流路内での電解質溶液の移動装置。

【請求項4】請求項1及び2に記載の一对の電極に印加される電圧は、電解質溶液が移動する上流側の電極孔に設けた電極は接地電位に、下流側の電極孔に設けた電極には電圧を印加することを特徴とした溝流路内での電解質溶液の移動装置。

【請求項5】請求項4に記載の下流側の電極に印加される電圧は－電圧であることを特徴とした溝流路内での電解質溶液の移動装置。

【請求項6】請求項2に記載の珪素基板を加工し、当該溝流路と複数本溝群を形成後に酸化膜の厚さを変えて当該複数本溝群の溝間の幅を変化させることを特徴とする溝流路内での電解質溶液の移動装置。

【請求項7】請求項1及び2に記載の一对の電極のうち、電解質溶液が流れる上流側の電極に銀／塩化銀電極を用い、封止することを特徴とする溝流路内での電解質溶液の移動装置。

【請求項8】請求項1及び2に記載の当該複数本溝群が間隔を置いて直列に配置されることを特徴とする溝流路内での電解質溶液の移動装置。

【請求項9】請求項1及び2に記載の当該複数本溝群は当該溝流路の幅より広く配置され、且つ当該溝流路と接続されていることを特徴とする溝流路内での電解質溶液の移動装置。

【請求項10】請求項2に記載の当該流路、および複数本溝群はSOI (Silicon on Insulator) 基板上的珪素層に形成されることを特徴とする溝

流路内での電解質溶液の移動装置。

【請求項11】請求項2と10に記載の珪素基板、および珪素層に当該溝流路と複数本溝群の形成に際して、フッ素原子を含むガスを用いた反応性イオンエッチングと、フロロカーボンガスと水素の混合ガスを用いて浮遊電位でフロロカーボン膜の溝内の均一な堆積と、フッ素原子を含むガスを用いた反応性イオンエッチングによる底部堆積膜の除去と、珪素のエッチングと、酸素プラズマによる溝内堆積膜の除去からなる一サイクルを多数回繰り返すことによって当該構造を形成することを特徴とする溝流路、および複数本溝群形成の方法。

【請求項12】請求項2と10に記載の珪素基板、および珪素層に当該溝流路と複数本溝群の形成に際して、請求項11の溝流路、および複数本溝群のエッチング形成後、全ての溝の側壁に生じた波状の疎表面に、フッ素原子を含むガスに当該ガス濃度の2.5倍以上の酸素を混合したガスを2.45GHzのマイクロ波で放電せしめ、生じた活性ガス種をプラズマが存在しない下流域に輸送して暴露することを特徴とする珪素溝流路、および複数本珪素溝群の側壁の平滑化の方法。

【請求項13】請求項12に記載の珪素溝流路の平滑化後、珪素溝を含む全ての珪素表面を酸化する際、ウェット酸化を行うことを特徴とする溝流路、および複数本溝群形成の方法。

【請求項14】同一の電解質溶液に浸漬したときに、当該溶液との界面での界面動電位が互いに異なるような複数の基板材料を用いた部品を組み合わせ構成した液体の成分分析装置。

【請求項15】複数の基板部品を組み合わせ構成した液体の成分分析装置であって、当該複数の基板の中の一部の基板の表面の少なくとも一部が表面処理を施され、特にこの表面処理後の表面を同一の電解質溶液に浸漬したときの当該溶液との界面での界面動電位が表面処理前の基板材料のそれと異なることを特徴とする液体の成分分析装置。

【請求項16】請求項14に記載の基板材料の一つとして、特に珪素酸化物を主成分として含むものを用いることを特徴とする液体の成分分析装置。

【請求項17】請求項14に記載の基板材料の一つとして、特に珪素を主成分として含むものを用い、かつ当該珪素基板表面が酸化されていることを特徴とする液体の成分分析装置。

【請求項18】請求項15に記載の表面処理が珪素酸化膜の被覆であることを特徴とする液体の成分分析装置。

【請求項19】請求項18に記載の珪素酸化膜が少なくとも珪素を構成元素として含む分子の気体と酸素を構成元素として含む分子の気体のプラズマ処理を用いて形成されることを特徴とする液体の成分分析装置ならびに液体の成分分析装置の製造方法。

【請求項20】請求項15に記載の表面処理が表面を構

成する分子の酸化処理に伴う改質であることを特徴とする液体の成分分析装置ならびに液体の成分分析装置の製造方法。

【請求項21】請求項15に記載の表面処理を施す基板材料がプラスチックであることを特徴とする液体の成分分析装置。

【請求項22】請求項16に記載の珪素酸化物を主成分として含む基板材料の他に、基板材料として少なくともプラスチックが用いられていることを特徴とする液体の成分分析装置。

【請求項23】請求項17に記載の表面に酸化層が形成されている珪素を主成分とする基板材料の他に、基板材料としてプラスチックが用いられていることを特徴とする液体の成分分析装置。

【請求項24】請求項21乃至23に記載のプラスチックが、特にポリエチレンテレフタレート（PET）であることを特徴とする液体の成分分析装置。

【請求項25】請求項21乃至23に記載のプラスチックが、特にポリカーボネート（PC）であることを特徴とする液体の成分分析装置。

【請求項26】請求項14および15に記載の液体は特に水素イオン濃度が中性（pHが7程度）であることを特徴とする液体の成分分析装置。

【請求項27】請求項14および15に記載の液体は、特に血液であることを特徴とする液体の成分分析装置。

【請求項28】請求項27に記載の液体の成分分析装置が、生体内より血液を採取する採取手段と、少なくとも採取した当該血液をろ過し血漿を得るろ過手段あるいは当該血液から血清を分離する分離手段の内いずれかの手段と、当該血液中の物質を分析する分析手段と、当該採取手段、当該ろ過手段、当該分離手段、当該分析手段を接続する流路手段と、当該採取手段、当該ろ過手段、当該分離手段、当該分析手段、当該流路手段内に存在する当該血液の成分を移動させる移動手段と、当該分析手段からの情報を外部に取出すための出力手段と、当該採取手段、当該ろ過手段、当該分離手段、当該分析手段、当該移動手段、当該出力手段の少なくとも一つの手段の動作を制御するための制御手段を備えることを特徴とする液体の成分分析装置。

【請求項29】請求項28に記載の種々の手段の内、少なくとも移動手段を含むいくつかの手段とその他の手段は、一旦異なる基板上にそれぞれ形成された後にそれらを貼り付け、一体化されていることを特徴とする液体の成分分析装置ならびに液体の成分分析装置の製造方法。

【請求項30】請求項29に記載の少なくとも移動手段を含むいくつかの手段を形成する基板材料が、特に珪素酸化物を主成分として含むものを用いることを特徴とする液体の成分分析装置。

【請求項31】請求項29に記載の少なくとも移動手段を含むいくつかの手段を形成する基板材料が、特に珪素

を主成分として含むものを用い、かつ当該珪素基板表面が酸化されていることを特徴とする液体の成分分析装置。

【請求項32】請求項29に記載の少なくとも移動手段を含むいくつかの手段を形成する基板材料が、特にプラスチックであり、かつ少なくとも移動手段部分の一部表面は主として珪素酸化物膜で被覆されていることを特徴とする液体の成分分析装置。

【請求項33】請求項29に記載の少なくとも移動手段を含むいくつかの手段を形成する基板材料が、特にプラスチックであり、かつ少なくとも移動手段部分の一部表面は主として珪素酸化物膜で被覆されていることを特徴とする液体の成分分析装置。

【請求項34】請求項29に記載の少なくとも移動手段を含むいくつかの手段の表面の少なくとも一部が、表面を構成する分子の酸化処理に伴う改質を施されていることを特徴とする液体の成分分析装置。

【請求項35】請求項33及び34に記載のプラスチックは、特にポリエチレンテレフタレートであることを特徴とする液体の成分分析装置。

【請求項36】請求項33及び34に記載のプラスチックは、特にポリカーボネートであることを特徴とする液体の成分分析装置。

【請求項37】請求項29に記載の少なくとも移動手段を含むいくつかの手段以外の手段を形成する基板内の種々の手段の少なくとも一部の表面は、生体適合性を有する有機分子で被覆されていることを特徴とする液体の成分分析装置ならびに液体の成分分析装置の製造方法。

【請求項38】請求項29に記載の生体適合性を有する有機分子が、特にMPC（2-methacryloyloxyethylphorylcholine）ポリマーであることを特徴とする液体の成分分析装置。

【請求項39】請求項29に記載の生体適合性を有する有機分子が、特にポリエチレングルコースであることを特徴とする液体の成分分析装置。

【請求項40】請求項29に記載の種々の手段を形成した基板同士の貼り付け、一体化に伴う基板境界の各手段の接続は、その他の手段間の接続面内と直角方向に流路を形成して行うことを特徴とする液体の成分分析装置ならびに液体の成分分析装置の製造方法。

【発明の詳細な説明】

【0001】

【発明の属する技術分野】本発明は、石英板や高分子板などの絶縁材基板に作製した超小型の溝流路によって構成されたマイクロキャピラリと呼ばれているチップ装置とその製造方法と、当該キャピラリ内に電解質溶液を移動させるために低い電圧で駆動させるポンプ装置およびその製造方法に関する。特に微量（1マイクロリットル以下）の血液などの電解質溶液をキャピラリ内に注入し、これをキャピラリ中のバイオセンサー上に移動さ



せ、その成分分析測定を行い、血液の場合にはこの測定結果から人間の健康状態を診断する検査診断機構及び装置と電解質溶液を移動させる電気浸透流ポンプ装置に関する。

【0002】

【従来の技術】従来の健康や疾病状態は、数ccの多量の血液を採取し、その分析に大規模な自動血液分析装置で得た測定値より診断されてきた。しかし、近年、極度に進歩した半導体装置作製に用いられる微細加工技術を応用し、ただか数mmから数cm四方のチップ上に種々の分析器、分析装置を配置して、そこに被験者の血液などの体液を導き、被験者の健康状態を瞬時に把握することができる新しいデバイスの開発とその実用化の気運が高まってきている。これはこのような安価なデバイスの出現により、来たるべき高齢化社会において老人の日々の健康管理を在宅で可能にすることなどで増加の一端を辿る健康保険給付金の圧縮を図れることや救急医療の現場においては被験者が感染症（肝炎、後天性免疫不全症など）などを保持しているか否かを本デバイスを用いて迅速に判断できれば適切な対応ができるなど、種々の社会的な効果が期待されるために非常に注目されつつある技術分野である。

【0003】通常、このような自動分析装置は、病院などの医療機関に設置されており、規模が大きく、また、その操作は専門の資格を有するものに限られるのもであった。ところが、近年、このような自動分析装置に替わって、血液分析を各家庭で自らの手で実施することを目指した小型簡便な血液分析方法ならびに血液分析装置が開発されている（特願2000-120189）。

【0004】図1にこのような血液分析装置の一例を示す。101は基板であり、以下に示す本装置の各手段はマイクロキャピラリによって構成される。102は血液の採取手段である。103は中空の針であり、採取手段に付属する。この針を体内に刺して基板内への血液の取り入れ口とする104、105は電極であり、この電極間に印加した電圧のため生じる電気浸透流による吸引力によって、体内より基板内に血液を取り入れる。106は血液の濾過手段であり、血液の流れの上流から下流に向かって、次第に間隔の狭くなる複数のスリットを有する。このスリットにより、血液中の赤血球、白血球、リンパ球、血小板を濾過して取り除き、濾過手段の下流側に血漿を得る。107は分離手段であり、例えばU字型のマイクロキャピラリからなる。採取した血液を濾過して得られる血漿をこのU字型のマイクロキャピラリに導いた後、本基板を遠心分離器により一定方向に加速度を加えることによって、U字部に血漿より凝固因子を分離除去した血清が得られる。108は分析手段であり、血液中のpH値、酸素、二酸化炭素、ナトリウム、カリウム、カルシウム、グルコース、乳酸などの各濃度を測定するためのセンサを有する。109は採取手段、濾過手

段、分離手段、分析手段のそれぞれを接続する流路手段であり、基板をエッチングして製作したマイクロキャピラリからなる。110はマイクロキャピラリ中で血液を電気浸透流により移動させるための移動手段である。111は分析手段から情報を取出すための出力手段であり、電極などから構成される。112は、以上の採取手段、濾過手段、分離手段、分析手段、移動手段、出力手段を必要に応じて制御するための制御手段である。図示していないが、基板上のマイクロキャピラリ内に血液を保持しておくための保持手段を有し、この板は基板101に接着あるいは圧着されている。

【0005】採取手段102により採取された血液は、濾過手段104にて濾過され血漿となり、さらに分離手段105にて凝固因子を分離除去して血清が得られ、これを分析手段においてpH値、酸素、二酸化炭素、ナトリウム、カリウム、カルシウム、グルコース、乳酸などの各濃度を測定する。各手段間の血液の移動は、電気泳動法を用いた移動手段110により行う。

【0006】このような血液分析装置の基板には石英などのガラス材料が用いられることが多かったが、装置を大量にまた費用を抑えて製作するのに適するものとして、樹脂素材が用いられるようになってきている。

【0007】また、図1で述べた移動手段110は、超小型マイクロキャピラリチップに血液を引き込んだり、バイオセンサーの校正用の溶液を導入するために用いられ、超小型で且つ低電力駆動のポンプで構成される。従来の超小型ポンプは、マイクロマシン技術によってダイヤフラムをピエゾ素子で駆動したものが主であるが、その他、キャピラリ内にメッシュ電極を入れ、これに高DC電圧を印加して電解質溶液中の電荷を有する分子を駆動して溶液を移動させるものや、キャピラリ内に電極アレーを挿入して、それに位相シフトさせながら矩形波の電圧を印加して、電解質溶液を移動させるものなどがある。

【0008】

【発明が解決しようとする課題】樹脂素材を基板として用いた場合には、血液血清成分要素を含むほぼ中性の溶液を浸したときの表面の界面動電位（ゼータ電位）の絶対値が比較的低いために、電気浸透流を利用する移動手段110におけるポンプ作用の能力が低下するという問題が生じている。一方では、採取手段102、濾過手段106、分離手段107、分析手段108、流路手段109の全血あるいは血清が接触する部分ではたんぱく質や血球の付着を抑えるために生体適合性を有する有機材料、例えばMPC（2-methacryloyloxyethylphosphorylcholine）ポリマー、ポリエチレングリコール（PEG）の直鎖を表面に有する高分子ミセルなどを表面に被覆する必要がある。これらの生体適合膜の効果については既に特願2000-116091において述べられている。

【0009】これらの問題を解決するために、特願2000-116091においては図1に示したような同一樹脂基板上の種々の手段中の採取手段102、濾過手段106、分離手段107、分析手段108、流路手段109の表面は生体適合性を有する有機材料で被覆し、その一方で移動手段110の表面は中性の電解質溶液を浸したときの表面のゼータ電位の絶対値が大きい材料、例えば珪素酸化物で部分的に被覆したり、プラズマ処理によって当該移動手段表面を構成する樹脂の改質を図りゼータ電位の絶対値を向上させる方法が示されている。しかしこれらの方法の場合、所望の部位に所望の材料の被覆あるいは表面改質を行う必要があるが、もともと基板上の各々の手段の大きさがマイクロメートルのオーダーであるため精度良くこのような表面の被覆の仕分けや表面処理を行うことが難しいという問題があった。

【0010】また従来用いられている超小型ポンプのダイヤフラム駆動は複雑な構造であり、ダイヤフラムに寿命もあり、材質によっては血液や電解質溶液を汚染させることも懸念される。また、その他の溶液を移動させる部位に電極を設けることは製作上そう容易でなく、同じ汚染の問題もある。本発明が目指す在宅で健康状態を診断できるチップは使い捨てが可能で安価なものでなければならぬが、従来の方法は安価とは云えず、更に高電圧や高周波を必要とするため、人が在宅で使用するには安全とは云えない。本発明の目的は、微量血液を極細針を用いてマイクロキャピラリチップに注入するために、構造が簡単で、且つ低電圧駆動で強力に電解質溶液を移動させることができる電気浸透流ポンプ装置を提供することにある。

【0011】

【課題を解決するための手段】上で述べたような従来技術の所望の部位に所望の材料の被覆あるいは表面改質を行う際の問題点は、同一の基板上に様々な手段を形成し、これらの表面の一部に適宜必要な表面処理を施していることから派生したものである。本発明の発明者らは必要な表面処理ごとに多く手段をの分け、それらごとに用いる基板を変えてこれらの手段をそれぞれ形成し、必要な表面処理を施した後にこれらの基板を貼り合わせて一体化し、血液分析装置を構成すればよいと考えた。例えば図1においては採取手段102、濾過手段106、分離手段107、分析手段108、流路手段109等の手段と、移動手段110を各々異なる基板上に独立に作製し、しかるべき表面被覆や表面改質などをそれぞれの基板に対して施した後に両者を貼り付け一体化する。このようにすることによって表面被覆や表面改質を従来のように局所的に行う必要がなくなり、特殊な手間の必要とされる被覆あるいは改質装置および方法が必要とされないという利点がある。

【0012】具体的にはまず、移動手段110以外の採取手段102、濾過手段106、分離手段107、分析

手段108、流路手段109等の手段は廉価な樹脂製の基板上に形成する。このときこれら手段を構成する表面の少なくとも一部はMPCポリマー等の生体適合性を有する材料で被覆しておく。一方、移動手段110は前述の樹脂製基板よりも表面積の小さい基板上に形成する。このとき少なくとも移動手段110を構成する表面の少なくとも一部は、中性領域の電解質溶液を浸したときにゼータ電位の絶対値が、前述の樹脂製基板上に形成した種々の手段の表面のそれよりも高い材料で構成される。そしてこれらの樹脂製の基板と移動手段110が形成されている基板を貼り合わせて一体化する。このとき樹脂基板上の分析手段108と、当該樹脂基板より表面積の小さい基板上の移動手段110の間には流路が確実に接続されている。以上のようにすることによって、採取手段102、濾過手段106、分離手段107、分析手段108、流路手段109等の手段においては血液成分に含まれるタンパク質や種々の血球などの付着が抑制されて、血液血清成分は滞りなくこれらの手段を通過することができ、また、移動手段110の表面の少なくとも一部は、中性領域の電解質溶液を浸したときにゼータ電位の絶対値が、前述の樹脂製基板上に形成した種々の手段の表面のそれよりも高い材料で構成されることから、電気浸透流を移動手段として用いる場合、低い電極間電位で高い引き込み、あるいは押し出し能力を得ることができる。

【0013】また、本発明の一部の基となる電気浸透流の原理を図2を用いて簡単に説明する。201は石英板であり、石英表面202は通常水酸基で覆われているが、電解質溶液203を石英製キャピラリ204に注入すると、水素イオンが電解質溶液中に移動し、その結果、石英の表面には負の電荷205が生じ、電解質溶液中のカチオン（陽イオン）206が表面に移動し、ヘルムホルツの電気二重層207を生じる。この電位をゼータ電位と呼び、その電位の大きい方が電気浸透流が大きく、石英は特にその電位が高い。そこで、キャピラリの両端に正208と負209の高電圧を印加すると、そのカチオンが負電圧側に流れ、その粘性流210により電解質溶液自体が負電圧方向に移動する現象が電気浸透流である。従って、このような石英製キャピラリを流路の一部に接続し、キャピラリの両端にのみ電圧を印加して、流路共に電解質溶液で満たすと、そのキャピラリに流れる電気浸透流によって流路全体に電解質溶液を移動させることができる。この石英製キャピラリに相当するものが電気浸透流ポンプと呼んでいる。しかし、図2のような流路の一部に電圧を印加するだけでは、電解質溶液を移動させるためには、従来、数百から数千Vも必要であった。一方、電気浸透流ポンプ能力に相当する電解質溶液を移動させる圧力は、キャピラリの断面にほぼ反比例するので、カチオンの付着を増すために幅が広く、溶液は流れ易くするために長さは短く、ポンプ部分のみ

に高電界が印加させるために狭いギャップの構造が必要になる。

【0014】

【発明の実施の形態】図3に本発明に基づく装置の概略図を示す。図中で図1と同じものは、図1と同じ番号で示す。採取手段102、分離手段107、分析手段108、流路手段109等の手段は樹脂基板A303と樹脂基板B304の間に形成され、これらの表面はMPCポリマーで被覆しておく。一方、移動手段110は基板A306と基板B307の間に形成され、少なくとも当該移動手段の表面の少なくとも一部は中性領域の電解質溶液を浸したときにゼータ電位の絶対値が、前述の樹脂製基板上に形成した種々の手段の表面のそれよりも高い材料で構成される。これは基板自体にこのようにゼータ電位の高い材料を用いても良いし、基板に安価な樹脂を用いてその表面をゼータ電位の高い材料で被覆しても良いし、表面改質処理によりゼータ電位を向上させても良い。このような処理を施した後に樹脂基板A303と樹脂基板B304、および基板A306と基板B307を貼り合わせて一体化する。このとき流路接続部302においては樹脂基板A303と基板B307に貫通させた孔を合致させながら貼り合わせることで分析手段108と移動手段110の間の流路を接続することができる。

【0015】図4に本発明の電気浸透流ポンプの構造の概略図を示す。401は石英板などの絶縁材板、または珪素基板であり、402はマイクロキャピラリとなる溝流路であり、その一部に403の多数本からなる深い溝群を形成し、404と405は其々注入口と放出口である。珪素基板の場合は、まず402と403を加工形成後、酸化する。図5は、図4で示した溝が形成された基板の蓋501であり、石英基板、または珪素基板を酸化したものである。401と501を接着する。502と503は其々404と405に対応して、電解質溶液の注入口と放出口用の孔であり、504と505は其々電極であり、線状の白金などの金属やAg/AgCl電極、または金属薄膜である。

【0016】次に、図4に構造において本発明のポンプ作用を起す様子を、図6を用いて説明する。まず、電解質溶液が流れる溝流路全体601の一部に、溝幅は狭く、深さは溝流路と同じ深さで、その溝を多数本設けた溝群602を形成する。そして、溝流路全体に電解質溶液を満たし、この複数本溝群の両側に、603と604の電極から電圧を印加すると、この溝群以外の605と606ではイオンが流れ易く、溝群の部分602では流れ難く、抵抗は極めて高くなる。従って、溝群の両端に印加電圧の大部分が集中し、その結果、図6に示すように電界607は、溝群内の狭い溝ギャップには高電界が印加されることになるので、溝に付着したカチオンが印加した電圧が低くても移動し易くなる。

【0017】

【実施例】【第一の実施例】図2において樹脂基板A、B、Cの材料としてポリエチレンテフタレート（PET）を用い、また基板材料A、Bの材料として石英を用いて、それぞれの基板上に採取手段102、分離手段107、分析手段108、流路手段109等の手段と電気浸透流を用いた移動手段110を形成し、PET基板上の各手段の表面にはMPCポリマーを被覆した後に、PET基板と石英基板を貼り合わせ一体化し、血液分析装置を構成する。移動手段内のみにリン酸緩衝液を満たし、電気浸透流を用いて、実際に採取手段102から血液を引き込み、分離手段107で血清血球分離を行い、血清成分を分析手段に導くことを試みたところ血液および血液成分の移動が問題なく、石英基板のみを用いて作製した場合よりも短時間に行えることを確認した。石英基板のみの場合よりも短時間に移動させることができるのは、図1の採取手段102、分離手段107、分析手段108、流路手段109のみにMPCポリマーを被覆する工程で、わずかながらMPCポリマーを含む溶媒が移動手段110まで浸透し、ここが一部MPCポリマーで被覆されてしまいゼータ電位が低下したためであると考えられる。このように本発明によって必要な表面状態によって用いる基板を複数にすることでこのような表面処理に伴う問題を抑制しながら液体の移動手段を含む分析装置を安価に作製することができる。また、珪素基板を熱酸化して計粗層下層が形成されている表面に移動手段110を形成し、これと採取手段102、分離手段107、分析手段108、流路手段109等の手段を形成したPET基板と貼り付け一体化した場合においてもほぼ同じ様な良好な結果が得られた。

【0018】【第二の実施例】第一の実施例中で用いた石英基板の代わりに安価なプラスチックであるPETを基板として用い、これに移動手段を形成した後、この内壁表面への珪素酸化膜被覆を目的に、移動手段内に珪素を構成元素として含む分子としてTEOS（テトラエトキシシラン、 $\text{Si}(\text{OC}_2\text{H}_5)_4$ ）、また酸素を構成元素として含む分子として酸素を希釈剤としてのヘリウム（He）とともに導入し、移動手段の基板外側に電極を設置して、これに高周波（周波数：13.56MHz）を5W印加して、移動手段内大気圧下でマイクロプラズマを生成した。本処理を1分間行った後に、採取手段102、分離手段107、分析手段108、流路手段109を形成したPET基板と貼り合わせて一体化し、血液分析装置を形成する。実際に採取手段102から血液を引き込み、分離手段107で血清血球分離を行い、血清成分を分析手段に導くという、血液および血液成分の移動が問題なく行えることを確認した。また同様に移動手段内にヘリウムで希釈した酸素ガスを導入し、マイクロプラズマ処理を施した後においてもTEOSを導入して内壁に珪素酸化膜を被覆した場合とほぼ同等の血液および血液成分の移動特性が得られた。これは内壁表面

が酸素プラズマにより酸化されるような表面改質処理によって表面を構成する分子が分極した結果、高いゼータ電位が得られたことによると考えられる。さらにPETの代わりにやはり安価なプラスチック材料であるポリカーボネイト(PC)を用いた場合にも、PETのときと同様に良好な結果が得られた。

【0019】〔第三の実施例〕図4に示したような電気浸透流ポンプを作製し、性能を調べた。作製法は、石英板と珪素基板を用い、石英板の場合は、石英板表面にクロム(Cr)膜を1.5μmの厚さでスパッタ堆積した。珪素の場合は、珪素基板を1000℃でウェット酸化して、800nmの熱酸化膜を形成した。石英板の場合はCr膜上、珪素の場合は酸化膜上に、電子ビームレジスト(ZEP7000)を約700nmスピン塗布し、電子ビーム描画機でパターンを形成した。それをマスクに、Cr膜の場合は、塩素+30%酸素の混合ガスをICP(誘導結合プラズマ)を1巻きアンテナ型に13.56MHzの高周波電力を500kWで投入し、アンテナから19cmの下流の位置でDCバイアス印加用に13.56MHzの高周波と結合した水冷基盤にウェハを載置して、120eVのイオンエネルギーでCr膜をエッチングした。このCr膜をマスクに、C<sub>4</sub>F<sub>8</sub>+70%SF<sub>6</sub>のICPを用いて下地の石英基板をエッチングした。

【0020】熱酸化膜の場合は、C<sub>4</sub>F<sub>8</sub>+40%H<sub>2</sub>を用い、ICPの1巻きアンテナに13.56MHzの高周波電力を600kWで投入し、DCバイアス印加用に13.56MHzの高周波と結合した水冷基盤にウェハを載置して、300eVのイオンエネルギーでこのレジストマスクでエッチングした。レジストを除去後、酸化膜をマスクにして下地のSi基板を改良ボッシュ法でエッチングした。通常のボッシュ法は、(1)SF<sub>6</sub>などのプラズマでSiを等方形状にエッチング、(2)CHF<sub>3</sub>などのプラズマにより等方形状の内壁にフッロカーボン膜を堆積、(3)アルゴンプラズマ中で基盤に高周波バイアスを印加して、Ar<sup>+</sup>イオンを衝撃し、底面の堆積膜のみを除去の一サイクルを多数回繰り返して、Si基板の深堀(ディープ)エッチングを行うが、Ar<sup>+</sup>イオンにより熱酸化膜がスパッタエッチングされ、耐マスク性が悪かった。そこでこの改良として、図7にその工程を示すように、まず(1)珪素酸化膜701をマスクにしてSF<sub>6</sub>を用いたRIE(反応性イオンエッチング)を行うと、アンダーカット702が生じるが、底部703はアンダーカット量より多くエッチングされる。ここで、704は珪素基板である。(2)C<sub>4</sub>F<sub>8</sub>+20%H<sub>2</sub>を用いて浮遊電位でフッロカーボン膜705を溝内に均一に堆積させる。(3)再び(1)のプロセスにより底部堆積膜を除去する同時に、下地の珪素基板704をエッチングする。(4)O<sub>2</sub>プラズマにより溝内堆積膜を除去する。この工程から成る一サイ

クルを多数回繰り返し、珪素基板を深くエッチングする。しかし、703のアンダーカットに起因して、本質的に溝側壁に波形状が発生する。そこで、CF<sub>4</sub>+300%O<sub>2</sub>を用いた2.45GHzのマイクロ波放電で生じたフッ素原子と過剰な酸素原子によってダウンフローでこの溝を処理して、波形状の平滑化を行う。当該プロセス後、珪素の溝を含む全表面を酸化する。その際、O<sub>2</sub>を用いたドライ酸化では、図8(イ)に示すように、溝の開口部には酸化膜が盛り上がり形成されるが、蒸留水の蒸気と酸素の混合ガスや、酸素と水素の混合ガスのパイロジェニック反応によって生じた水を高温の電気炉に導入して珪素を酸化するウェット酸化法を用いると、図8(ロ)に示すように溝内が均一に酸化される事が判明した。

【0021】こうして形成した珪素溝を1000℃で10分と13分の二種類のウェット酸化をした。この溝流路と溝群から成るチップと、電極孔を超音波ドリルで開けた石英板とを1%フッ酸溶液中に浸漬して、1.3MPaの圧力を24時間印加して接着した。これはフッ酸ボンディングと呼んでいる。石英基板の場合は、1μm以下の幅の深溝の製作は困難だったので、図9は、珪素基板に製作した電気浸透流ポンプを用いて性能を調べたときの構成図を示す。幅0.5mm、深さ10μmの溝流路901の両側の直径1.5mmの電極孔にAg/AgCl電極902と白金電極903を設け、その間の0.5mm×0.5mm領域に、0.85μm(a)と0.6μm(b)の二種類のギャップ、深さ10μmのSiO<sub>2</sub>/Si溝を316列に設けた溝群ポンプ部904を作製した。902のAg/AgCl電極には、+電圧を印加し、903の白金電極には-電圧を印加した。Ag/AgCl電極を用いた理由は、低電圧の印加では電解質溶液を電気分解して水素を発生する現象が無いからである。従って、電解質溶液の流れは902から903に向かって流れるので、902の孔からの空気の流れを防ぐため、Ag/AgCl電極を挿入後、接着剤で孔を封じた。902と903の孔の間隔は3mmであり、結局3mm×10μm×0.5mmの容積の電解質溶液を負荷として移動させた。電解質溶液としては、イオン強度が1/10、pHが7.4のPBS(リン酸緩衝液)を用いた。当該ポンプを用いて、血液を905の注入口からキャピラリ906に引き込み、参照電極907とバイオセンサー、例えばISFET(イオン敏感電界型トランジスタ)908により健康マーカーを測定する際、ISFETのゲート絶縁膜の静電破壊や当該ポンプに印加した電位の影響を防ぐためには、902のAg/AgCl電極は接地電位にする。

【0022】図10は、この珪素基板製のポンプを用い、流量(ナノリットル/秒)と印加電圧の関係を示す。(a)は、溝間のギャップが0.85μmの場合であり、10Vまではほぼ線形的に流量が増加し、その後

10

20

30

40

50

飽和の傾向を示した。これは、Siを酸化した膜の厚さが200nmなので、10Vの印加でその酸化膜には $5 \times 10^4$  V/cmの電界が印加されたため、酸化膜の電流リークか一部の絶縁破壊が生じ、印加電圧が低下したためと考えられる。しかし、10Vの電圧で前記容積のPBSが0.5ナノリットル/秒の流速が得られ、これは、水を25mmの高さに押し上げる力がある。耐圧劣化は酸化膜厚を厚くすることで改善でき、(b)は、溝間のギャップが0.6μmの場合であり、耐圧と流量の両方とも向上している。この溝群型を縦型と呼ぶと、比較として、図10中に幅1mm、長さ100μm、ギャップ0.85μm平板型と呼ぶ構造の電気浸透流ポンプを石英板にドライエッチング加工して作製した結果を(c)として示した。その結果、同じギャップの0.85μmの場合のポンプ力を比較すると、縦型は平面型と比べて10Vの印加電圧で約10倍優れていると考えられる。

【0023】〔第四の実施例〕図4の縦型の平面部も利用するため、縦型と図10中に示した平板型を組み合わせた構造のものを図11に示す。この場合、電解質溶液は紙面と垂直方向に流れる。1101は溝流路と溝群を形成する石英などの絶縁板や珪素基板、1102は溝群、1103は石英などの絶縁板や珪素基板であり、その一部に平板の溝1104が加工されている。珪素基板の場合は前述同様、酸化を行う。1101と1103の基板の接着には前述のフッ酸ボンディングを行う。当該構造により、図2の単なる溝型に比べて約10%のポンプ力を増加させることができた。

【0024】図12は、本実施例の変形であり、はじめに石英板のような絶縁材基板や珪素基板に、平板型の溝1201を形成し、その中に多数本溝群1202を形成止、絶縁材基板1203で蓋をする。効果は図9の構造と同じであった。

【0025】〔第五の実施例〕図13は、更にポンプ力を増すため、図4に示した多数本溝群を複数個にして間隔をあけて直列に接続した構造を示す。1301は溝流路、1302と1303は電極孔、1304は溝群、1305は血液などを引き込む負荷としてのキャピラリ流路である。複数個の当該溝と同じ長さの溝を用いてもポンプ力は当然向上するが、イオン電流がこのような長い溝を流れると、ジュール加熱が起り、ポンプが破損したり、細い溝に異物が詰まることがある。従って、これらの問題は、溝構造を分割し、直列にすることで解決できた。

【0026】〔第六の実施例〕図14は、ポンプ力の向上を目指し、図4の溝構造において、溝群の溝数を増し、更に図10と同様直列に間隔をあけて接続したポンプ構造を示す。1401は溝流路、1402と1403は電極孔、1404は溝数を増した溝群、1405は1401の溝流路から1404の多数本溝群へ電解質溶液

がスムーズに流し、且つ電界を緩やかに印加するためのテーパー構造、1406は血液などを引き込む負荷としてのキャピラリ流路である。本実施例では、単一の多数本溝群を図13と同様に、複数個を直列に接続することにより、更に大きなポンプ力を得ることが出来た。

【0027】〔第七の実施例〕図10に示した珪素溝を酸化した構造の結果では、酸化膜の耐圧が悪いと、電流リークなどで電圧印加に対してポンプ力が飽和する。この原因は、酸化膜にリークが生じるということは、電解質溶液と下地の珪素基板の電位が接近、又は同じになることを意味する。これを防止するには、珪素基板が電気的に浮遊していればよく、そのため、SOI(Silicon on Insulator)基板を用いた溝構造を図15に示す。図15において、1501は珪素基板、1502は珪素酸化膜、1503は珪素層、1504は珪素酸化膜、1505は溝群、1506は珪素酸化膜の蓋である。当該SOI基板を用いることで、耐圧を更に大きくすることができ、20Vを印加しても図16に示すように飽和すること無く、線形的に流量が増加した。

【0028】

【発明の効果】以上説明したとおり、本発明により複数の基板を組み合わせることで安価に高性能な血液を含む電解質溶液の成分分析装置を実現することができた。また、当該装置の重要な構成要素である電気浸透流ポンプの高性能化を達成することができた。これにより在宅で微量血液から健康状態などを診断するデバイスを安価、且つ人体に安全に用いることが可能になった。さらに本発明は血液のみには止まらず、微量液体の成分分析装置にも寄与している。

【図面の簡単な説明】

【図1】 従来装置を説明する図である。

【図2】 本発明の一部の基となる電気浸透流の原理の説明する図である。

【図3】 本発明による装置の概略図である。

【図4】 本発明の溝流路と複数本溝群からなる電気浸透流ポンプの構造の概略図である。

【図5】 図4で示した溝流路と複数本溝群が形成された基板の絶縁材料の蓋であり、電解質溶液の注入口と放出口用に其々電極を挿入した構造を示す。

【図6】 図2に構造において本発明の複数本溝群に強力な電気浸透流作用を生じる基となる複数本溝のギャップに強い電界が生じることを説明する図である。

【図7】 珪素基板に深い溝を形成するボッシュ法を改良したエッチング法として、当該4工程を一サイクルとして多数回繰り返すエッチングプロセスを説明する図である。

【図8】 珪素溝を酸化する際、(イ)はO<sub>2</sub>ドライ酸化、(ロ)はウェット酸化によって酸化膜が形成される様子の違いを示した図である。

【図9】 珪素基板に製作した多数本溝群による電気浸透流ポンプの性能を調べるための構成図を示している。

【図10】 珪素基板に製作した多数本溝群による電気浸透流ポンプ（ここでは縦型と呼んでいる）を用い、流量と印加電圧の関係を示す。（a）は、溝間のギャップが0.85μmと0.6μmの場合であり、（c）は図中に示した平面型の構造の特性を示している。

【図11】 縦型と平板型を組み合わせた構造のポンプを示している。

【図12】 図11の変型例を示す図である。

【図13】 多数本溝群を複数個にして間隔をあけて直列に接続しポンプ力増強を図った構造を示している。

【図14】 図4の溝構造において、溝群の溝数を増し、更に図10と同様直列に間隔をあけて接続ポンプ力増強を図った構造を示している。

【図15】 SOI（Silicon on Insulator）基板を用いた珪素層に多数本溝群を形成した際に珪素酸化膜にリークが存在しても高電圧が印加できるポンプ構造を示している。

【図16】 図15に示した多数本溝群を用いた電気浸透流特性を示す図である。

【符号の説明】

101 基板  
102 採取手段  
103 針  
104 電極  
105 電極  
106 濾過手段  
107 分離機構  
108 分析手段  
109 流路手段  
110 移動手段  
111 出力手段  
112 制御手段  
201 石英板  
202 石英表面  
203 電解質溶液  
204 石英製キャピラリ  
205 負の電荷  
206 カチオン  
207 ヘルムホルツの電気二重層  
208 正の電極  
209 負の電極  
210 粘性流  
301 液貯め  
302 流路接続部  
303 樹脂基板A  
304 樹脂基板B  
305 樹脂基板C  
306 基板A

10

20

30

40

50

307 基板B  
401 石英板  
402 溝流路  
403 溝群  
404 注入口  
405 放出口  
501 蓋  
502 注入口用の孔  
503 放出口用の孔  
504 電極  
505 電極  
601 溝流路全体  
602 溝群  
603 電極  
604 電極  
605 溝群以外の溝流路  
606 溝群以外の溝流路  
607 電界  
701 珪素酸化膜  
702 アンダーカット  
703 底部  
704 珪素基板  
705 フロロカーボン膜  
801 珪素酸化膜  
802 珪素基板  
901 溝流路  
902 Ag/AgCl電極  
903 白金電極  
904 溝群ポンプ部  
905 注入口  
906 キャピラリ  
907 参照電極  
908 ISFET  
1101 基板  
1102 溝群  
1103 基板  
1104 溝  
1201 溝  
1202 多数本溝群  
1203 基板  
1204 基板  
1301 溝流路  
1302 電極  
1303 電極  
1304 溝群  
1305 キャピラリ流路  
1401 溝流路  
1402 電極  
1403 電極  
1404 溝群

17

18

1405 テーパ構造

1406 キャピラリ流路

1501 珪素基板

1502 珪素酸化膜

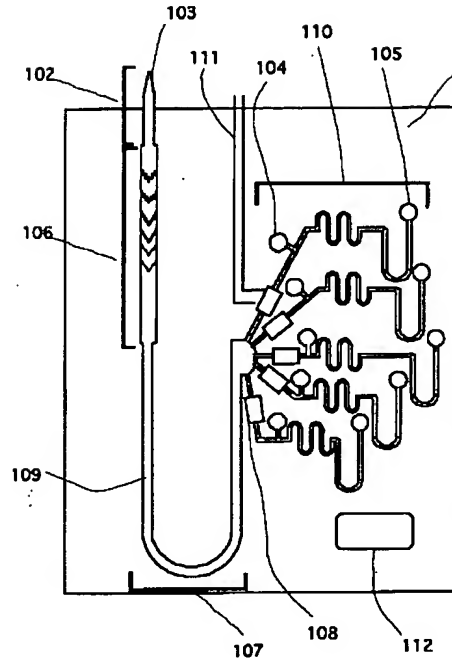
\* 1503 珪素層

1504 珪素酸化膜

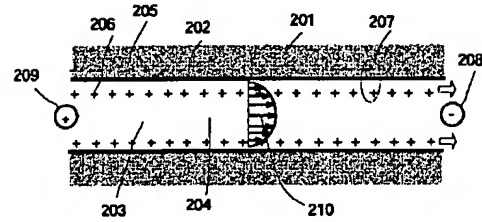
1505 溝群

\* 1506 珪素酸化膜の蓋

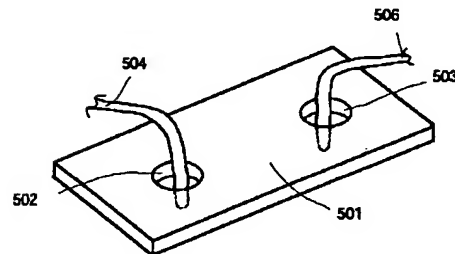
【図1】



【図2】

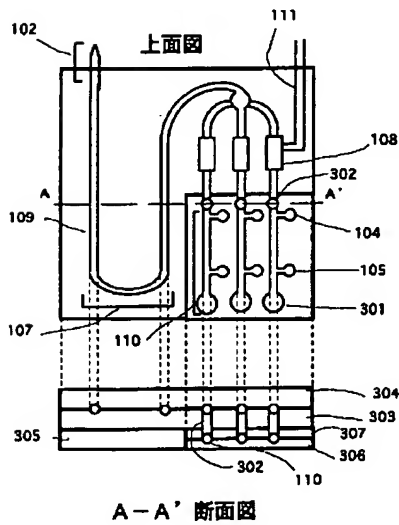


【図5】

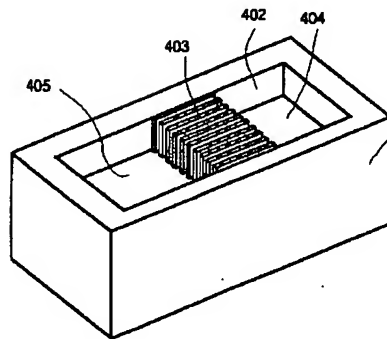


【図9】

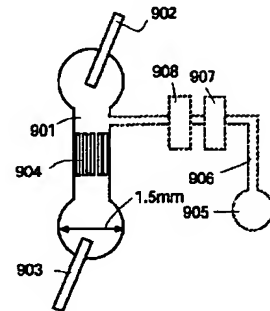
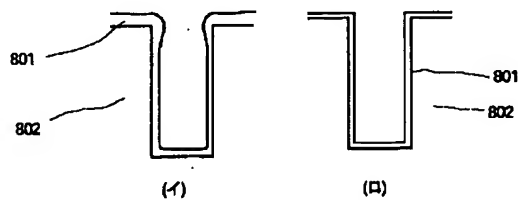
【図3】



【図4】

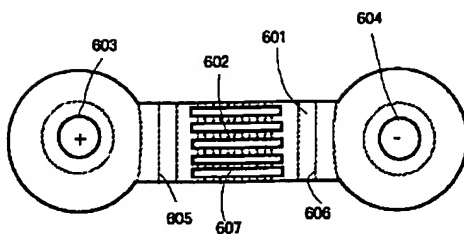


【図8】

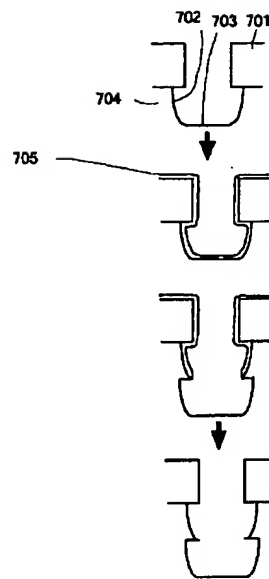




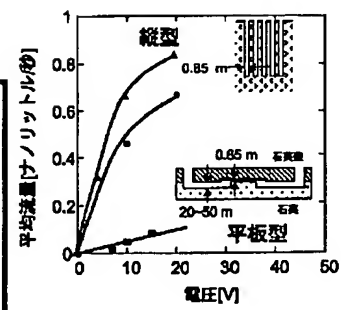
【図6】



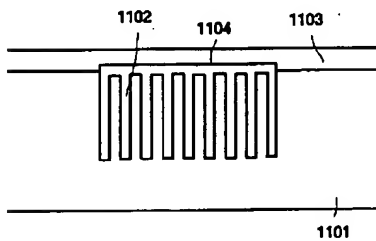
【図7】



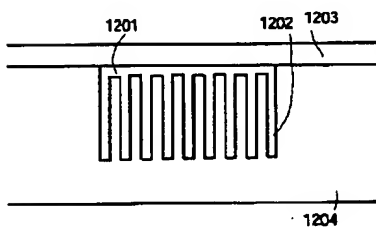
【図10】



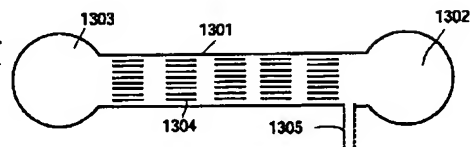
【図11】



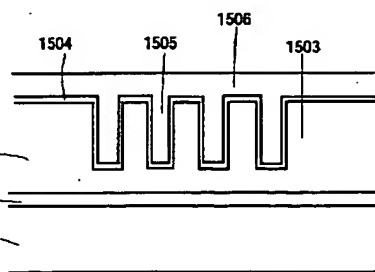
【図12】



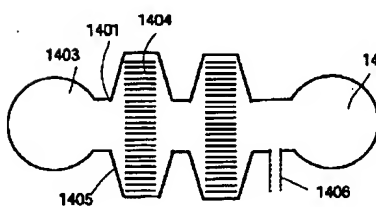
【図13】



【図15】

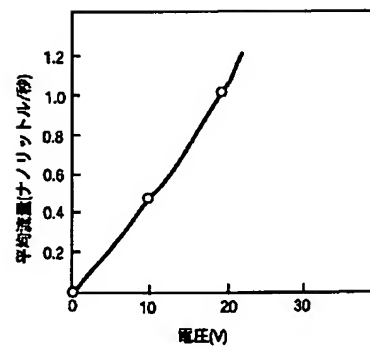


【図14】





〔図16〕




---

フロントページの続き

(51)Int.Cl. <sup>7</sup>	識別記号	F I	テーマコード(参考)
G 0 1 N 33/84		G 0 1 N 27/46	3 3 8
		27/26	3 3 1 E
(72)発明者 高村 禪		F ターム(参考)	2G045 AA13 AA25 BA08 BA10 BB05
東京都荒川区南千住四丁目9番地2	リバ		BB10 CA25 CA26 DA04 DA31
ーハープ南千住 401号			DB01 DB03 DB07 DB09 DB10
(72)発明者 小川 洋輝			FA05 FA34 FB05
神奈川県横浜市港北区新横浜2丁目18番地		2G052	AA30 AB01 AB02 AB06 AD09
1 センチュリー新横浜701号室			AD29 AD46 BA14 CA02 CA03
(72)発明者 菊地 純			CA04 CA07 ED17 JA01
東京都港区白金台2丁目14番地6号			